tion. Interfering with hnRNP I results in developmental defects in *Drosophila* and amphibian. We characterized the adult phenotype of brom bones, a zebrafish mutant deficient in hnRNP I, and found that hnRNP I plays a novel role in regulating intestinal homeostasis. Brom bones display a number of defects in the intestinal epithelium, including abnormal cell lineage development, uncontrolled intestinal cell growth, and a markedly increased Notch signaling activity. Our biochemical analysis demonstrates that hnRNP I inhibits Notch signaling by controlling the stability of the intracellular domain of Notch (NICD). In addition to its role in the adult intestine, we found that hnRNP I is expressed in the developing digestive system in the zebrafish embryo. Morpholino knockdown of hnRNP I in zebrafish embryos impairs the development of multiple digestive organs, including the liver, pancreas and intestine. Our results demonstrate that hnRNP I plays important roles in the digestive organ development and adult intestinal homeostasis.

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Program/Abstract # 219
Tubular extension and cell epithelialization are coordinately regulated and influenced by adjacent tissues
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Epithelial tubules are essential functional components in major organs of the body. When a tubular structure forms during development, cells undergo epithelialization and robust extension. We have asked how these morphological events are coordinated in three-dimensional environment. To address these questions, we have recently developed a novel model using Wolffian duct (WD, also called a nephric duct), the earliest basis for kidney formation. WD is a simple structure, and extends in an anterior-to-posterior direction as a straight cord. Time-lapse imaging analyses revealed that cells located at the extending-front (tip region) are actively motile with numerous filopodia whereas cells residing in the rear region are epithelial in shape with less motility. Remarkably, when replaced into the front region, the rear cells can be converted to the front cell-like and restarted to extend posteriorly. These observations suggest that tissues surrounding the front region play instructive roles in the tubular extension. To further elucidate the molecular mechanisms underlying the tubular extension, we investigated the role of the chemokine SDF-1. SDF-1 (ligand) is expressed in tissues adjacent to the front cells of WD, which express the receptor CXCR4. When ectopically administered, SDF-1 attracted WD cells, suggesting that the WD extension is controlled by interactions between the neighboring tissues where SDF-1/CXCR4 signals instruct the front cells.

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Program/Abstract # 220
Wnt4 induces tubule formation in metanephric mesenchyme by a non-canonical mechanism
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Wnt4 and βcatenin are both required for nephrogenesis, but studies of TCF-reporter mice suggest that canonical activation does not occur in metanephric mesenchyme (MM) during its conversion to nephronic epithelia. To study the mechanism, we developed a model that permits progenitor propagation in primary explant culture. Using this, we found that recombinant Wnt4 protein induces tubule formation and differentiation markers *Lim1* and *E-cadherin* in MM cells but does not activate a TCF reporter or expression of canonical Wnt target gene axin2 and minimally affects stabilization of βcatenin, which remains phosphorylated. Furthermore, Wnt4 caused localization of ZO1 and occludin to tight junctions. On the other hand, canonical activation with a TCF-βcatenin fusion construct, stabilization of βcatenin with a proteasomal inhibitor, or treatment of cells with a Wnt agonist, all of which activated a TCF reporter, were unable to induce tubule formation, and canonical Wnt inhibitor dkk1 could not block differentiation. Since a canonical mechanism is not operative in tubule formation, we assessed the role of non-canonical mechanisms with small molecule inhibitors. Both CaMKII and JNK inhibitors blocked tubule formation, and treatment of MM cells with Wnt4 caused a rapid activation of CaMKII and JNK. These results demonstrate that the canonical Wnt pathway is not responsible for mesenchymal–epithelial transition in nephron formation and suggest that both the non-canonical calcium–Wnt and the JNK-mediated Wnt/PCP pathways are involved in Wnt4-induced tubulogenesis in the kidney.

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Program/Abstract # 221
Tissue interactions during formation of the pronephric duct in *Xenopus laevis*
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In *Xenopus laevis* embryos, formation of the excretory system occurs in three temporally distinct phases: From stages 22 to 26 the pronephros and pronephric duct (PD) rudiments can be observed segregating from intermediate mesoderm directly ventral to somites IV–IX; from stage 29–33 cell migration extends the PD posteriorly from the level of somite IX to somite XIV; from stages 30 to 38 rectal diverticulae (RD) extend anteriorly from the cloaca to meet and fuse with the PD ventral to somite XIV. We have performed a set of tissue extirpation and tissue marking experiments to 1) investigate the tissue interactions required for maintenance and elongation of PD and RD tissue, and 2) determine whether cells from tissues other than the PD primordium contribute to the elongating PD. Tissue extirpation studies show that the epidermis is essential for maintenance of the PD and that removal of the PD does not prevent anterior extension of the RD, but is required for subsequent RD maintenance. Tissue marking studies indicate that neural crest does not contribute cells to the PD during PD elongation; removal of trunk neural crest results in foreshortening of the embryo but does not interfere with PD elongation. In addition, the width of the PD does not decrease as the PD elongates, indicating that the embryo can regulate PD size and may recruit cells from surrounding tissues.

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Program/Abstract # 222
A role for GDNF in pronephric duct cell migration in *Xenopus laevis*
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Anterior to posterior extension of the *Xenopus* pronephric duct (PD) is complex, consisting of three distinct temporal phases: During the first phase, pronephric and PD tissue segregates from flank mesoderm directly ventral to somites IV–VIII; during the second phase, cells migrate throughout the duct extending it to the axial level of somite XIV; finally, anterior extension of rectal diverticulae (RD) from the cloaca to the posterior tip of the PD is required to